

Application No.: 09/954,571

2

Docket No.: 220002066000

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

Please cancel claims 46 to 51, 56, 59 and 60, without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Claim 1 (previously presented): A method for delivering a therapeutic dose of an expression cassette to cardiac muscle comprising steps of:

(a) providing a viral vector comprising an [[the]] expression cassette comprising a sequence encoding a mutated form of the phospholamban (PLB) gene; and

(b) ~~inducing complete or near-complete transient cardiac arrest or reversible bradycardia in the cardiac muscle;~~

(c) ~~administering a vascular permeabilizing agent to the cardiac muscle; and~~

(d) ~~administering the viral vector to the cardiac muscle.~~

Claim 2 (previously presented): The method of claim 1, further comprising the induction of hypothermia in the cardiac muscle.

Claim 3 (previously presented): The method of claim 1, further comprising isolation of the cardiac muscle from systemic circulation.

Claim 4 (previously presented): The method of claim 1, further comprising induction of hypothermia in the cardiac muscle and isolation of the cardiac muscle from systemic circulation.

Claim 5 (canceled)

Claim 6 (previously presented): The method of claim 1, further comprising induction of reversible bradycardia.

sd-246709

Application No.: 09/954,571

3

Docket No.: 220002066000

Claim 7 (previously presented): The method of claim 1, wherein the vascular permeabilizing agent comprises histamine, substance P or serotonin.

Claim 8 (previously presented): The method of claim 1, wherein at least one bolus of viral vector is administered to the cardiac muscle.

Claim 9 (previously presented): The method of claim 1, wherein the viral vector comprises an adenoviral vector.

Claim 10 (previously presented): The method of claim 9, wherein the adenoviral vector comprises a cardiac specific promoter.

Claim 11 (previously presented): The method of claim 9, wherein the adenoviral vector comprises a cytomegalovirus (CMV) promoter.

Claim 12 (previously presented): The method of claim 9, wherein the adenoviral vector comprises a Rous sarcoma virus (RSV) promoter.

Claim 13 (previously presented): The method of claim 9, wherein the adenoviral vector comprises an enhancer.

Claim 14 (previously presented): The method of claim 13, wherein the enhancer comprises a cytomegalovirus (CMV) enhancer.

Claim 15 (previously presented): The method of claim 13, wherein the enhancer comprises a Rous sarcoma virus (RSV) enhancer.

Claim 16 (previously presented): The method of claim 1, wherein the viral vector comprises an adenovirus-associated viral (AAV) vector.

sd-246709

Application No.: 09/954,571

4

Docket No.: 220002066000

Claim 17 (previously presented): The method of claim 16, wherein the AAV vector comprises a cardiac specific promoter.

Claim 18 (previously presented): The method of claim 16, wherein the adenovirus-associated viral (AAV) vector comprises a cytomegalovirus (CMV) promoter.

Claim 19 (previously presented): The method of claim 16, wherein the adenoviral vector comprises a Rous sarcoma virus (RSV) promoter.

Claim 20 (previously presented): The method of claim 16, wherein the adenovirus-associated viral (AAV) vector comprises an enhancer.

Claim 21 (previously presented): The method of claim 20, wherein the enhancer comprises a cytomegalovirus (CMV) enhancer.

Claim 22 (previously presented): The method of claim 20, wherein the enhancer comprises a Rous sarcoma virus (RSV) enhancer.

Claims 23 to 30 (canceled)

Claim 31 (previously presented): The method of claim 1, wherein the gene expression cassette comprises a gene fragment.

Claims 32 to 40 (canceled)

Claim 41 (previously presented): The method of claim 1, wherein the viral vector is in a fluid.

sd-246709

Application No.: 09/954,571

5

Docket No.: 220002065000

Claim 42 (previously presented): The method of claim 9, wherein the adenoviral vector is a replication deficient adenoviral vector.

Claim 43 (previously presented): The method of claim 16, wherein the adenovirus-associated viral (AAV) vector is a replication deficient adenovirus-associated viral (AAV) vector.

Claim 44 (previously presented): The method of claim 1, wherein the vascular permeabilizing agent and the viral vector, or, the vascular permeabilizing agent or the viral vector, are administered by myocardial perfusion.

Claim 45 (previously presented): The method of claim 44, wherein vascular permeabilizing agent or the viral vector is administered before or during, or, before and during, the myocardial perfusion.

Claims 46 to 51 (canceled)

Claim 52 (previously presented): The method of claim 1, wherein the expression cassette comprises a mutated form of a gene.

Claim 53 (previously presented): The method of claim 52, wherein the mutated gene is a mutated phospholamban (PLB) that enhances sarco-endoplasmic reticulum calcium ATPase (SERCA-2) activity.

Claim 54 (previously presented): The method of claim 53, wherein the mutated gene is a dominant negative form of phospholamban (PLB).

Claim 55 (previously presented): The method of claim 52, wherein the mutated gene is a dominant negative form of phospholamban (PLB) comprising a mutation at amino acid 16 from serine (S) to glutamic acid (E).

sd-246709

Application No.: 09/954,571

6

Docket No.: 220002066000

Claim 56 (canceled)

Claim 57 (previously presented): The method of claim 54, wherein the mutated gene is a dominant negative form of phospholamban (PLB).

Claim 58 (previously presented): The method of claim 55, wherein the mutated gene is a dominant negative form of phospholamban (PLB) comprising a mutation at amino acid 16 from serine (S) to glutamic acid (E).

Claims 59 and 60 (canceled)

Claim 61 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene regulating cardiac function.

Claim 62 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene for treating cardiac disease.

Claim 63 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene for treating heart failure.

Claim 64 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene regulating cardiac contractility and relaxation.

Claim 65 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene regulating calcium handling in cardiomyocytes.

Claim 66 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene regulating calcium uptake into sarco-endoplasmic reticulum in cardiac cells.

sd-246709

Application No.: 09/954,571

7

Docket No.: 220002066000

Claim 67 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene encoding sarco-endoplasmic reticulum calcium ATPase (SERCA-2).

Claim 68 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene encoding a polypeptide binding to sarco-endoplasmic reticulum calcium ATPase (SERCA-2) in cardiac cells.

Claim 69 (previously presented): The method of claim 1, wherein the expression cassette comprises a gene encoding a polypeptide that regulates sarco-endoplasmic reticulum calcium ATPase (SERCA-2) in cardiac cells.

Claim 70 (new): A method of delivering a therapeutic dose of a gene to the heart for treating cardiac disease, wherein the gene comprises a mutated form of a phospholamban (PLB) gene, and the method comprises the step of administering a viral vector comprising the mutated PLB gene to the heart.

Claim 71 (new): The method of claim 70, wherein the gene is administered in a gene expression cassette.

Claim 72 (new): The method of claim 71, wherein the gene expression cassette comprises a promoter.

Claim 73 (new): The method of claim 72, wherein the promoter is a cytomegalovirus (CMV) promoter.

Claim 74 (new): The method of claim 72, wherein the promoter is a Rous sarcoma virus (RSV) promoter.

sd-246709

Application No.: 09/954,571

8

Docket No.: 220002066000

Claim 75 (new): The method of claim 71, wherein the gene expression cassette comprises an enhancer.

Claim 76 (new): The method of claim 75, wherein the enhancer is a cytomegalovirus (CMV) enhancer.

Claim 77 (new): The method of claim 70, wherein the viral vector is an adenovirus-associated viral vector (AAV).

Claim 78 (new): The method of claim 70, further comprising administering a sarcoplasmic reticulum Ca²⁺ ATPase (SERCA-2) gene.

Claim 79 (new): The method of claim 70, wherein the PLB gene is a dominant negative PLB gene.

Claim 80 (new): The method of claim 79, wherein the PLB gene comprises a mutation of E2A.

Claim 81 (new): The method of claim 79, wherein the PLB gene comprises a mutation of R14E.

Claim 82 (new): The method of claim 79, wherein the PLB gene comprises a mutation of S16N.

Claim 83 (new): The method of claim 79, wherein the PLB gene comprises a mutation of S16E.

Claim 84 (new): The method of claim 79, wherein the PLB gene comprises a mutation of V49A.

sd-246709

Application No.: 09/954,571

9

Docket No.: 220002066000

Claim 85 (new): The method of claim 79, wherein the PLB gene comprises a mutation of K3E and R14E.

Claim 86 (new): The method of claim 70, wherein the mutated dominant negative PLB gene enhances SERCA-2 activity.

sd-246709